

March 10, 2023

Lu Cai, Michael Horowitz, Md., Shahidul Islam, and Jian-Bo Xiao

Editors-in-Chief

World Journal of Diabetes

Dear Editor:

We wish to re-submit the manuscript titled "Early Diabetic Kidney Disease: Focus on the Glycocalyx." The manuscript ID is 82167.

We thank you and the reviewers for your thoughtful suggestions and insights. The manuscript has benefited from these insightful suggestions. I look forward to working with you and the reviewers to move this manuscript closer to publication in the *World Journal of Diabetes*.

Research has shown that approximately half of all patients with diabetic kidney disease (DKD) will eventually develop end-stage renal disease (ESRD), and this will create serious health and economic burdens for countries, societies, and individuals. It is thus imperative that methods are developed to delay or prevent the progression of DKD at an early stage. This review has discussed current research relating to early DKD development and the importance of the glycocalyx. We have thoroughly evaluated the structural and functional alterations that occur to the glycocalyx due to DKD, the mechanisms of damage, and available therapies. The aim was to highlight the advances that have been made in this field as well as the areas that should be the focus of further investigation in the future. It is hoped that this review will provide guidance and help facilitate research in the future that will lead to the development of treatments for early DKD and thus help to improve patient quality of life and life expectancy.

Further, we believe that this review will be suitable for your journal as it directly relates to diabetes and has a global perspective. The content should be of interest to your readers and specifically help to guide their research and bring new students to this field up to speed.

This manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal. We have read and understood your journal's policies, and we believe that neither the manuscript nor the study violates any of these. There are no conflicts of interest to declare.

The manuscript has been rechecked and the necessary changes have been made in accordance with the reviewers' suggestions. The responses to all comments have been prepared and attached herewith.

Reviewer#1

Specific comments: In this paper, the authors reviewed the pathogenesis of diabetic kidney disease, especially focusing on Identifying and targeting the key molecules involved in glycocalyx damage. The paper is interesting and suitable for the journal.

Reply: Thanks for your comments.

Reviewer#2

Specific comments: In this manuscript, the authors have evaluated "Early Diabetic Kidney Disease: Focus on the Glycocalyx" Overall, this Manuscript provides valuable and valid data. I do not see any major issues in this Manuscript; the Manuscript can only be accepted after minor revision. A few minor issues need to be addressed, as pointed below: 1-The manuscript must be carefully proofread for grammar, spelling, and punctuation issues. 2-There is no balance between the different sections of the manuscript. The content of the abstract was too long.

Reply: In terms of language, we carefully proofread grammar, spelling, abbreviations, and punctuation and submitted it to the English polishing company for a new round of polishing to make the language quality meet the publication requirements. In view of the imbalance between different parts of the content, first of all, various endothelial glycocalyx components have different research efforts in diabetic kidney disease. We have collected relatively more data for hot issues and described them in more detail. As for the areas that have yet to be thoroughly studied, we also make a brief description. Even so, we felt room for improvement in the content. Therefore, we made cuts and additions, combined narratives, and structural adjustments to some content to maintain a balance between different parts of the article. Especially for the abstract part, we have deleted some of the redundant content and highlighted the structure and function of the endothelial glycocalyx, the mechanism of its damage, and the therapeutic targets, making the content clearer and the central idea more concise. In addition, we also add more general points to the conclusion section, such as "endothelial glycocalyx homeostasis" and "the interaction between podocytes and endothelial cells", to make the ending more complete and convincing.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

Xian-Hua Li, MD, PhD, Chief Doctor, Professor

Department of Nephrology, Qilu Hospital of Shandong University, 107

Wenhua Xi Road, Jinan, Shandong 250012, China

lixianhua7075@sina.com